Consequences of ionizing radiation-induced damage in human neural stem cells.

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Public Summary:

Scientific Abstract:
Cranial irradiation remains a frontline treatment for brain cancer, but also leads to normal tissue damage. Although low-dose irradiation (</=10 Gy) causes minimal histopathologic change, it can elicit variable degrees of cognitive dysfunction that are associated with the depletion of neural stem cells. To decipher the mechanisms underlying radiation-induced stem cell dysfunction, human neural stem cells (hNSCs) subjected to clinically relevant irradiation (0-5 Gy) were analyzed for survival parameters, cell-cycle alterations, DNA damage and repair, and oxidative stress. hNSCs showed a marked sensitivity to low-dose irradiation that was in part due to elevated apoptosis and the inhibition of cell-cycle progression that manifested as a G2/M checkpoint delay. Efficient removal of DNA double-strand breaks was indicated by the disappearance of gamma-H2AX nuclear foci. A dose-responsive and persistent increase in oxidative and nitrosative stress was found in irradiated hNSCs, possibly the result of a higher metabolic activity in the fraction of surviving cells. These data highlight the marked sensitivity of hNSCs to low-dose irradiation and suggest that long-lasting perturbations in the CNS microenvironment due to radiation-induced oxidative stress can compromise the functionality of neural stem cells.